

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
18 August 2005 (18.08.2005)

PCT

(10) International Publication Number
WO 2005/075463 A1

(51) International Patent Classification⁷: **C07D 405/12**,
409/12, 311/58, A61K 31/352

(21) International Application Number:
PCT/EP2005/050275

(22) International Filing Date: 21 January 2005 (21.01.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
04075293.3 3 February 2004 (03.02.2004) EP

(71) Applicants (for all designated States except US): **UNIVERSITE DE LIEGE** [BE/BE]; Interface Entreprises Université, Université de Liège, quai Van Beneden, 25, B-4020 LIEGE (BE). **UNIVERSITE LIBRE DE BRUXELLES** [BE/BE]; avenue F.D. Roosevelt, 50, B-1050 Bruxelles (BE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **SEBILLE, Sophie** [BE/BE]; Rue Docteur Beaujean, 7 bte 4, B-4218 COUTHUIN (BE). **PIROTTE, Bernard** [BE/BE]; Rue Tollet, 5, B-4680 Oupeye (BE). **BOVERIE, Stéphane** [BE/BE]; La Rock, 19, B-4160 Anthistes (BE). **DE TULLIO, Pascal** [BE/BE]; Voie du HERDIER, 22, B-4020 Jupille-sur-Meuse (BE). **LEBRUN, Philippe** [BE/BE]; rue des chats, 102, B-1082 Bruxelles (BE). **ANTOINE, Marie-Hélène** [BE/BE]; rue Bollinckx, 17, B-1070 Bruxelles (BE).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,

GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

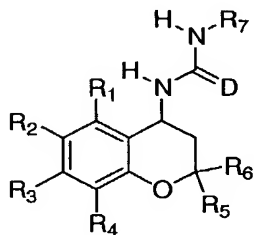
Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,

[Continued on next page]

(54) Title: BENZOPYRAN DERIVATIVES, METHOD OF PRODUCTION AND USE THEREOF



(I)

(57) Abstract: The invention relates to novel benzopyran derivatives of formula (I), to their method of production, to composition comprising the derivatives and use thereof. Formula (I) wherein: R₁, R₂, R₃ and R₄ are independently hydrogen, halogen, C₁₋₆-alkyl, C₃₋₈-cycloalkyl, hydroxy, C₁₋₆-alkoxy, C₁₋₆-alkoxy-C₁₋₆-alkyl, nitro, amino, cyano, cyanomethyl, perhalomethyl, C₁₋₆-monoalkyl- or dialkylamino, sulfamoyl, C₁₋₆-alkylthio, C₁₋₆-alkylsulfonyl, C₁₋₆-alkylsulfinyl, formyl, C₁₋₆-alkylcarbonylamino, R₈arylthio, R₈arylsulfinyl, R₈arylsulfonyl, C₁₋₆-alkoxycarbonyl, C₁₋₆-alkoxycarbonyl-C₁₋₆-alkyl, carbamoyl, carbamoylmethyl, C₁₋₆-monoalkyl- or dialkylaminocarbonyl, C₁₋₆-monoalkyl- or dialkylaminothiocarbonyl, ureido, C₁₋₆-monoalkyl- or dialkylaminocarbonylamino, thioureido, C₁₋₆-monoalkyl- or dialkylaminothiocarbonylamino, C₁₋₆-monoalkyl- or

dialkylaminosulfonyl, carboxy, carboxy-C₁₋₆-alkyl, acyl, R₈aryl, R₈aryl-C₁₋₆-alkyl, R₈aryloxy; R₅ and R₆ are each independently hydrogen, C₁₋₆-alkyl, R₅ and R₆ taken together with the carbon atom to which they are attached form a 3- to 6-membered carbocyclic ring; R₇ is 2-, 3- or 4-pyridyl optionally mono- or polysubstituted by R₁; R₇ is 2- or 3-thienyl optionally mono- or polysubstituted by R₁ or R₇ is phenyl optionally mono- or polysubstituted by R₁ with the exception of or R₇ representing C₆H₅; R₈ is hydrogen, halogen, C₁₋₆-alkyl, C₃₋₈-cycloalkyl, hydroxy, C₁₋₆-alkoxy, nitro, amino, cyano, cyanomethyl, perhalomethyl; or a salt thereof with a pharmaceutically acceptable acid or base, or any optical isomer or mixture of optical isomers, including a racemic mixture or any polymorphic and tautomeric form.

WO 2005/075463 A1



CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,

HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.